

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 3 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

AMEND THE ABOVE-IDENTIFIED APPLICATION AS FOLLOWS:

In The Claims:

Cancel claims 1266-1575.

Add new claims 1576-2142 as follows:

1576. (NEW) An array comprising a non-porous substrate having surfaces, each surface comprising at least one double-stranded nucleic acid fixed or immobilized thereto, wherein at least one nucleic acid strand or a sequence therefrom comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable, wherein at least one nucleic acid strand or a sequence therefrom in one of said surfaces is different from at least one other nucleic acid strand or a sequence therefrom in another surface, and wherein said non-porous substrate comprises siliceous matter or polymeric material.

1577. (NEW) The array of claim 1576, wherein said non-porous siliceous substrate comprises glass.

1578. (NEW) The array of claim 1577, wherein said glass is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 4 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1579. (NEW) The array of claim 1578, wherein said plate or plates comprise microtiter well plates.

1580. (NEW) The array of claim 1578, wherein said wells comprise microtiter wells.

1581. (NEW) The array of claim 1577, wherein said glass comprises porous glass or porous glass beads.

1582. (NEW) The array of claim 1576, wherein said non-porous polymeric substrate comprises plastic.

1583. (NEW) The array of claim 1582, wherein said plastic is selected from the group consisting of polyethylene, polypropylene, polystyrene and polyepoxide.

1584. (NEW) The array of claim 1582, wherein said plastic is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

1585. (NEW) The array of claim 1584, wherein said plate or plates comprises polystyrene plates.

1586. (NEW) The array of claim 1584, wherein said wells comprise microtiter wells.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 5 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1587. (NEW) The array of claim 1584, wherein said wells comprise polystyrene microfilter wells.

1588 (NEW) The array of claim 1584, wherein said wells comprise removeable wells.

1589. (NEW) The array of claim 1576, wherein said surface or surfaces have been treated with a surface treatment agent.

1590. (NEW) The array of claim 1589, wherein said surface treatment agent is selected from the group consisting of an amine compound and an epoxy resin or solution.

1591. (NEW) The array of claim 1590, wherein said amine compound comprises an amino-substituted hydrophobic polymer.

1592. (NEW) The array of claim 1590, wherein said amine compound is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution, and a combination of any of the foregoing.

1593. (NEW) The array of claim 1590, wherein said amine compound comprises polylysine (PPL).

1594. (NEW) The array of claim 1589, wherein said surface treatment agent comprises an epoxy resin or solution.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 6 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1595. (NEW) The array of claim 1576, wherein said surface or surfaces comprise one or more amine, polyamine, amino-substituted or amino-derivitized groups thereon.

1596. (NEW) The array of claim 1595, wherein said amine or polyamine result from a treatment of said surface or surfaces with a surface treatment agent.

1597. (NEW) The array of claim 1596, wherein said surface treatment agent is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

1598. (NEW) The array of claim 1576, wherein said at least one nucleic acid strand or a sequence therefrom has been fixed or immobilized to an amine or polyamine on said surface or surfaces.

1599. (NEW) The array of claim 1576, wherein said surface or surfaces have been treated with a blocking agent.

1600. (NEW) The array of claim 1599, wherein said blocking agent comprises Denhardt's solution.

1601. (NEW) The array of claim 1576, wherein said at least one nucleic acid strand or a sequence therefrom has been fixed or immobilized directly or indirectly to said surface or surfaces.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 7 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1602. (NEW) The array of claim 1576, wherein one strand of each of said double-stranded nucleic acid strands is fixed or immobilized directly or indirectly to said surface or surfaces.

1603. (NEW) The array of claim 1602, wherein said direct or indirect fixation or immobilization to said surface or surfaces is covalent or noncovalent.

1604. (NEW) The array of claim 1576, wherein said double-stranded nucleic acid strands are fixed or immobilized to said surfaces by sandwich hybridization.

1605. (NEW) The array of claim 1576, wherein said nucleic acid strands are selected from the group consisting of single-stranded nucleic acid and double-stranded nucleic acid.

1606. (NEW) The array of claim 1576, wherein said nucleic acid strands are selected from the group consisting of DNA, RNA and a DNA-RNA hybrid.

1607. (NEW) The array of claim 1576, wherein said at least one nucleic acid strand or a sequence therefrom comprises a nucleic acid sequence complementary to a nucleic acid sequence of interest or sought to be identified or quantified or sequenced.

1608. (NEW) The array of claim 1607, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced is isolated or derived from a biological or non-biological sample.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 8 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1609. (NEW) The array of claim 1608, wherein said biological sample comprises blood, urine, feces, saliva, pus, semen, serum or tissue,

1610. (NEW) The array of claim 1608, wherein said non-biological sample comprises fermentation broth or culture media.

1611. (NEW) The array of claim 1607, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises a member selected from the group consisting of a gene or gene sequence, a pathogen or pathogenic sequence, and a combination of any of the foregoing.

1612. (NEW) The array of claim 1607, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable.

1613. (NEW) The array of claim 1607, wherein said complementary nucleic acid sequence or sequences are unlabeled.

1614. (NEW) The array of claim 1576, wherein said non-radioactive chemical label or labels are the non-radioactive signaling moiety or moieties.

1615. (NEW) The array of claim 1576, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said array or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1616. (NEW) The array of claim 1614, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said array or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1617. (NEW) The array of claim 1576, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or a sequence therefrom.

1618. (NEW) The array of claim 1614, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or a sequence therefrom.

1619. (NEW) The array of claim 1576, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or a sequence therefrom.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 10 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1620. (NEW) The array of claim 1614, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or a sequence therefrom.

1621. (NEW) The array of claim 1619, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or a sequence therefrom.

1622. (NEW) The array of claim 1620, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or a sequence therefrom.

1623. (NEW) The array of claim 1621, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1624. (NEW) The array of claim 1622, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1625. (NEW) The array of claim 1623, wherein said bridging entity or complex is covalently or non-covalently attached.

1626. (NEW) The array of claim 1624, wherein said bridging entity or complex is covalently or non-covalently attached.

1627. (NEW) The array of claim 1625, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

1628. (NEW) The array of claim 1626, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

1629. (NEW) The array of claim 1576, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are covalently or non-covalently attached thereto.

1630. (NEW) The array of claim 1576, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are directly attached thereto.

1631. (NEW) The array of claim 1576, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are indirectly attached thereto.

1632. (NEW) The array of claim 1576, wherein said non-radioactive chemical label or labels comprise biotin, iminobiotin, a hapten or a ligand.

1633. (NEW) The array of claim 1576, wherein said non-radioactive chemical label or labels comprise indicator molecules.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 12 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1634. (NEW) The array of claim 1633, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1635. (NEW) The array of claim 1614, wherein said non-radioactive chemical label or labels comprise indicator molecules.

1636. (NEW) The array of claim 1635, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1637. (NEW) The array of claim 1576, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive signaling moiety or moieties.

1638. (NEW) The array of claim 1614, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive chemical label or labels.

1639. (NEW) The array of claim 1576, wherein said non-radioactive signaling moiety or moieties are directly produced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 13 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1640. (NEW) The array of claim 1639, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and a chemiluminescent compound.

1641. (NEW) The array of claim 1576, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1642. (NEW) The array of claim 1641, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

1643. (NEW) The array of claim 1642, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1644. (NEW) The array of claim 1643, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1645. (NEW) The array of claim 1644, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethylbenzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

1646. (NEW) The array of claim 1614, wherein said non-radioactive signaling moiety or moieties are directly produced.

1647. (NEW) The array of claim 1646, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and a chemiluminescent compound.

1648. (NEW) The array of claim 1614, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1649. (NEW) The array of claim 1648, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

1650. (NEW) The array of claim 1649, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1651. (NEW) The array of claim 1650, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1652. (NEW) The array of claim 1651, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzthiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

1653. (NEW) The array of claim 1576, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagenic compound, a fluorescent compound and a chemiluminescent compound.

1654. (NEW) The array of claim 1614, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagen compound, a fluorescent compound and a chemiluminescent compound.

1655. (NEW) The array of claim 1576, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

1656. (NEW) The array of claim 1614, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

1657. (NEW) The array of claim 1576, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 17 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1658. (NEW) The array of claim 1614, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

1659. (NEW) The array of claim 1657, wherein said colored compound comprises a dye.

1660. (NEW) The array of claim 1658, wherein said colored compound comprises a dye.

1661. (NEW) The array of claim 1576, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

1662. (NEW) The array of claim 1614, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

1663. (NEW) The array of claim 1661, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 18 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1664. (NEW) The array of claim 1662, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

1665. (NEW) The array of claim 1576, wherein said non-porous substrate is transparent or translucent.

1666. (NEW) The array of claim 1576, wherein said surfaces are transparent or translucent.

1667. (NEW) A collection or set comprising the arrays of any of claims 1576 to 1666.

1668. (NEW) A non-porous system which comprises the arrays of any of claims 1576 to 1666.

1669. (NEW) The system of claim 1668, wherein said system is transparent or translucent.

1670. (NEW) An array comprising a non-porous substrate having surfaces, each surface comprising at least one nucleic acid strand fixed or immobilized thereto, wherein at least one nucleic acid strand or a sequence therefrom in one of said surfaces is different from at least one other nucleic acid strand or a sequence therefrom in another surface, and wherein said non-porous substrate comprises siliceous matter or polymeric material.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 19 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1671. (NEW) The array of claim 1670, wherein said non-porous siliceous substrate comprises glass.

1672. (NEW) The array of claim 1671, wherein said glass is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

1673. (NEW) The array of claim 1672, wherein said plate or plates comprise microtiter well plates.

1674. (NEW) The array of claim 1672, wherein said wells comprise microtiter wells.

1675. (NEW) The array of claim 1671, wherein said glass comprises porous glass or porous glass beads.

1676. (NEW) The array of claim 1670, wherein said non-porous polymeric substrate comprises plastic.

1677. (NEW) The array of claim 1676, wherein said plastic is selected from the group consisting of polyethylene, polypropylene, polystyrene and polyepoxide.

1678. (NEW) The array of claim 1676, wherein said plastic is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection of said plates, wells, depressions, tubes, cuvettes or beads.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 20 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1679. (NEW) The array of claim 1678, wherein said plate or plates comprise polystyrene plates.

1680. (NEW) The array of claim 1678, wherein said wells comprise microtiter wells.

1681. (NEW) The array of claim 1678, wherein said wells comprise polystyrene microfilter wells.

1682. (NEW) The array of claim 1678, wherein said wells comprise removeable wells.

1683. (NEW) The array of claim 1670, wherein said surface or surfaces have been treated with a surface treatment agent.

1684. (NEW) The array of claim 1683, wherein said surface treatment agent is selected from the group consisting of an amine compound and an epoxy resin or solution.

1685. (NEW) The array of claim 1684, wherein said amine compound comprises an amino-substituted hydrophobic polymer.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 21 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1686. (NEW) The array of claim 1684, wherein said amine compound is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

1687. (NEW) The array of claim 1686, wherein said amine compound comprises polylysine (PPL).

1688. (NEW) The array of claim 1683, wherein said surface treatment agent comprises an epoxy resin or solution.

1689. (NEW) The array of claim 1670, wherein said surface or surfaces comprise one or more amine, polyamine, amino-substituted or amino-derivitized groups thereon.

1690. (NEW) The array of claim 1689, wherein said amine or polyamine result from a treatment of said surface or surfaces with a surface treatment agent.

1691. (NEW) The array of claim 1690, wherein said surface treatment agent is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

1692. (NEW) The array of claim 1670, wherein said at least one nucleic acid strand or a sequence therefrom has been fixed or immobilized to an amine or polyamine on said surface or surfaces.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 22 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1693. (NEW) The array of claim 1670, wherein said surface or surfaces have been treated with a blocking agent.

1694. (NEW) The array of claim 1693, wherein said blocking agent comprises Denhardt's solution.

1695. (NEW) The array of claim 1670, wherein said at least one nucleic acid strand or a sequence therefrom has been fixed or immobilized directly or indirectly to said surface or surfaces.

1696. (NEW) The array of claim 1695, wherein said direct or indirect fixation or immobilization to said surface or surfaces is covalent or noncovalent.

1697. (NEW) The array of claim 1670, wherein said nucleic acid strands are selected from the group consisting of single-stranded nucleic acid and double-stranded nucleic acid.

1698. (NEW) The array of claim 1670, wherein said nucleic acid strands are selected from the group consisting of DNA and RNA.

1699. (NEW) The array of claim 1670, wherein said at least one nucleic acid strand or a sequence therefrom comprises a nucleic acid sequence complementary to a nucleic acid sequence of interest or sought to be identified or quantified or sequenced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 23 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1700. (NEW) The array of claim 1699, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises a member selected from the group consisting of a gene or gene sequence, a pathogen or pathogenic sequence, and a combination of any of the foregoing.

1701. (NEW) The array of claim 1699, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable.

1702. (NEW) The array of claim 1699, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced is isolated or derived from a biological or non-biological sample.

1703. (NEW) The array of claim 1702, wherein said biological sample comprises blood, urine, feces, saliva, pus, semen, serum or tissue.

1704. (NEW) The array of claim 1702, wherein said non-biological sample comprises fermentation broth or culture media.

1705. (NEW) The array of claim 1699, wherein said complementary nucleic acid sequence or sequences are unlabeled.

1706. (NEW) The array of claim 1701, wherein said non-radioactive chemical label or labels are the non-radioactive signaling moiety or moieties.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 24 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1707. (NEW) The array of claim 1701, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said array or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1708. (NEW) The array of claim 1706, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said array or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1709. (NEW) The array of claim 1701, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or a sequence therefrom.

1710. (NEW) The array of claim 1706, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or a sequence therefrom.

1711. (NEW) The array of claim 1701, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or a sequence therefrom.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 25 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1712. (NEW) The array of claim 1706, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or a sequence therefrom.

1713. (NEW) The array of claim 1711, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or a sequence therefrom.

1714. (NEW) The array of claim 1712, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or a sequence therefrom.

1715. (NEW) The array of claim 1713, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1716. (NEW) The array of claim 1714, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1717. (NEW) The array of claim 1715, wherein said bridging entity or complex is covalently or non-covalently attached.

1718. (NEW) The array of claim 1717, wherein said bridging entity or complex is covalently or non-covalently attached.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 26 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1719. (NEW) The array of claim 1717, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

1720. (NEW) The array of claim 1718, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

1721. (NEW) The array of claim 1701, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are covalently or non-covalently attached thereto.

1722. (NEW) The array of claim 1701, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are directly attached thereto.

1723. (NEW) The array of claim 1701, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are indirectly attached thereto.

1724. (NEW) The array of claim 1701, wherein said non-radioactive chemical label or labels comprise biotin, iminobiotin, a hapten or a ligand.

1725. (NEW) The array of claim 1701, wherein said non-radioactive chemical label or labels comprise indicator molecules.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 27 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1726. (NEW) The array of claim 1725, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1727. (NEW) The array of claim 1706, wherein said non-radioactive chemical label or labels comprise indicator molecules.

1728. (NEW) The array of claim 1727, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1729. (NEW) The array of claim 1701, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive signaling moiety or moieties.

1730. (NEW) The array of claim 1706, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive chemical label or labels.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 28 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1731. (NEW) The array of claim 1729, wherein said non-radioactive signaling moiety or moieties are directly produced.

1732. (NEW) The array of claim 1731, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and chemiluminescent compound.

1733. (NEW) The array of claim 1729, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1734. (NEW) The array of claim 1733, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

1735. (NEW) The array of claim 1734, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1736. (NEW) The array of claim 1735, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1737. (NEW) The array of claim 1736, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

1738. (NEW) The array of claim 1706, wherein said non-radioactive signaling moiety or moieties are directly produced.

1739. (NEW) The array of claim 1738, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and chemiluminescent compound.

1740. (NEW) The array of claim 1706, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1741. (NEW) The array of claim 1740, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

1742. (NEW) The array of claim 1741, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1743. (NEW) The array of claim 1742, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1744. (NEW) The array of claim 1743, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzthiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 31 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1745. (NEW) The array of claim 1701, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagenic compound, a fluorescent compound and a chemiluminescent compound.

1746. (NEW) The array of claim 1706, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagen compound, a fluorescent compound and a chemiluminescent compound.

1747. (NEW) The array of claim 1701, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

1748. (NEW) The array of claim 1706, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

1749. (NEW) The array of claim 1701, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 32 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1750. (NEW) The array of claim 1706, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

1751. (NEW) The array of claim 1749, wherein said colored compound comprises a dye.

1752. (NEW) The array of claim 1750, wherein said colored compound comprises a dye.

1753. (NEW) The array of claim 1701, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

1754. (NEW) The array of claim 1706, wherein a non-radioactive signal from said non-radioactive chemical label or labels is quantifiable or detectable by photometric means.

1755. (NEW) The array of claim 1753, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 33 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1756. (NEW) The array of claim 1754, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

1757. (NEW) The array of claim 1670, wherein said non-porous substrate is transparent or translucent.

1758. (NEW) The array of claim 1670, wherein said surface or surfaces are transparent or translucent.

1759. (NEW) A collection or set comprising the arrays of any of claims 1670 to 1758.

1760. (NEW) A non-porous system which comprises the arrays of any of claims 1670 to 1758.

1761. (NEW) The system of claim 1760, wherein said system is transparent or translucent.

1762. (NEW) A non-porous system which comprises:

a non-porous solid support comprising comprising an activated surface; and
at least one double-stranded nucleic acid strand or a sequence fixed or
immobilized to said solid support surface covalently or non-covalently through said
activated surface, wherein said at least one double-stranded nucleic acid strand or
sequence comprises one or more non-radioactive chemical labels which comprise a
non-radioactive signaling moiety or moieties which are quantifiable or detectable.

1763. (NEW) The system of claim 1762, wherein said non-porous solid support
comprises siliceous matter or polymeric material.

1764. (NEW) The system of claim 1763, wherein said siliceous matter comprises
glass.

1765. (NEW) The system of claim 1764, wherein said glass is selected from the
group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a
collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

1766. (NEW) The system of claim 1765, wherein said plate or plates comprise
microtiter well plates.

1767. (NEW) The system of claim 1765, wherein said wells comprise microtiter
wells.

1768. (NEW) The system of claim 1764, wherein said glass comprises porous
glass or porous glass beads.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 35 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1769. (NEW) The system of claim 1763, wherein said polymeric material comprises plastic.

1770. (NEW) The system of claim 1769, wherein said plastic is selected from the group consisting of polyethylene, polypropylene, polystyrene and polyepoxide.

1771. (NEW) The system of claim 1769, wherein said plastic is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

1772. (NEW) The system of claim 1771, wherein said plate or plates comprises polystyrene plates.

1773. (NEW) The system of claim 1771, wherein said wells comprise microtiter wells.

1774. (NEW) The system of claim 1771, wherein said wells comprise polystyrene microfilter wells.

1775. (NEW) The system of claim 1771, wherein said wells comprise removeable wells.

1776. (NEW) The system of claim 1762, wherein said activated surface has been treated with a surface treatment agent.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 36 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1777. (NEW) The system of claim 1776, wherein said surface treatment agent is selected from the group consisting of an amine compound and an epoxy resin or solution.

1778. (NEW) The system of claim 1777, wherein said amine compound comprises an amino-substituted hydrophobic polymer.

1779. (NEW) The system of claim 1777, wherein said amine compound is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution, and a combination of any of the foregoing.

1780. (NEW) The system of claim 1777, wherein said amine compound comprises polylysine (PPL).

1781. (NEW) The system of claim 1776, wherein said surface treatment agent comprises an epoxy resin or solution.

1782. (NEW) The system of claim 1762, wherein said activated surface comprises one or more amine, polyamine, amino-substituted or amino-derivitized groups thereon.

1783. (NEW) The system of claim 1782, wherein said amine, polyamine, amino-substituted or amino-derivitized group or groups result from a treatment of said activated surface with a surface treatment agent.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 37 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1784. (NEW) The system of claim 1783, wherein said surface treatment agent is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

1785. (NEW) The system of claim 1762, wherein said at least one double-stranded nucleic acid strand or sequence has been fixed or immobilized to an amine or polyamine on said activated surface.

1786. (NEW) The system of claim 1762, wherein said activated surface has been treated with a blocking agent.

1787. (NEW) The system of claim 1786, wherein said blocking agent comprises Denhardt's solution.

1788. (NEW) The system of claim 1762, wherein said at least one nucleic acid strand or sequence has been fixed or immobilized directly or indirectly to said activated surface.

1789. (NEW) The system of claim 1762, wherein one strand of said at least one double-stranded nucleic acid strand or sequence is fixed or immobilized directly or indirectly to said activated surface.

1790. (NEW) The system of claim 1789, wherein said direct or indirect fixation or immobilization to said activated surface is covalent or noncovalent.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 38 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1791. (NEW) The system of claim 1762, wherein one strand of said at least one double-stranded nucleic acid or sequence is fixed or immobilized to said activated surface and the other strand is hybridized to said fixed or immobilized one strand.

1792. (NEW) The system of claim 1762, wherein said at least one double-stranded nucleic acid strand or sequence is fixed or immobilized to said activated surface by sandwich hybridization.

1793. (NEW) The system of claim 1762, wherein said at least one double-stranded nucleic acid strand or sequence is selected from the group consisting of DNA, RNA and a DNA-RNA hybrid.

1794. (NEW) The system of claim 1762, wherein said at least one nucleic acid strand or sequence comprises a nucleic acid sequence complementary to a nucleic acid sequence of interest or sought to be identified or quantified or sequenced.

1795. (NEW) The system of claim 1794, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced is isolated or derived from a biological or non-biological sample.

1796. (NEW) The system of claim 1795, wherein said biological sample comprises blood, urine, feces, saliva, pus, semen, serum or tissue.

1797. (NEW) The system of claim 1795, wherein said non-biological sample comprises fermentation broth or culture media.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 39 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1798. (NEW) The system of claim 1794, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises a member selected from the group consisting of a gene or gene sequence, a pathogen or pathogenic sequence, and a combination of any of the foregoing.

1799. (NEW) The system of claim 1794, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable.

1800. (NEW) The system of claim 1794, wherein said complementary nucleic acid sequence or sequences are unlabeled.

1801. (NEW) The system of claim 1762, wherein said non-radioactive chemical label or labels are the non-radioactive signaling moiety or moieties.

1802. (NEW) The system of claim 1762, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 40 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1803. (NEW) The system of claim 1801, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1804. (NEW) The system of claim 1762, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

1805. (NEW) The system of claim 1801, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

1806. (NEW) The system of claim 1762, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

1807. (NEW) The system of claim 1801, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

1808. (NEW) The system of claim 1806, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 41 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1809. (NEW) The system of claim 1807, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

1810. (NEW) The system of claim 1808, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1811. (NEW) The system of claim 1809, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1812. (NEW) The system of claim 1810, wherein said bridging entity or complex is covalently or non-covalently attached.

1813. (NEW) The system of claim 1811, wherein said bridging entity or complex is covalently or non-covalently attached.

1814. (NEW) The system of claim 1812, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

1815. (NEW) The system of claim 1813, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

1816. (NEW) The system of claim 1762, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are covalently or non-covalently attached thereto.

1817. (NEW) The system of claim 1816, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are directly attached thereto.

1818. (NEW) The system of claim 1762, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are indirectly attached thereto.

1819. (NEW) The system of claim 1762, wherein said non-radioactive chemical label or labels comprise biotin, iminobiotin, a hapten or a ligand.

1820. (NEW) The system of claim 1762, wherein said non-radioactive chemical label or labels comprise indicator molecules.

1821. (NEW) The system of claim 1820, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1822. (NEW) The system of claim 1801, wherein said non-radioactive chemical label or labels comprise indicator molecules.

1823. (NEW) The system of claim 1822, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1824. (NEW) The system of claim 1762, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive signaling moiety or moieties.

1825. (NEW) The system of claim 1801, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive chemical label or labels.

1826. (NEW) The system of claim 1762, wherein said non-radioactive signaling moiety or moieties are directly produced.

1827. (NEW) The system of claim 1826, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and a chemiluminescent compound.

1828. (NEW) The system of claim 1762, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1829. (NEW) The system of claim 1828, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 44 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1830. (NEW) The system of claim 1829, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1831. (NEW) The system of claim 1830, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1832. (NEW) The system of claim 1831, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

1833. (NEW) The system of claim 1801, wherein said non-radioactive signaling moiety or moieties are directly produced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 45 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1834. (NEW) The system of claim 1833, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and a chemiluminescent compound.

1835. (NEW) The system of claim 1801, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1836. (NEW) The system of claim 1835, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

1837. (NEW) The system of claim 1836, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1838. (NEW) The system of claim 1837, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1839. (NEW) The system of claim 1838, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzthiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

1840. (NEW) The system of claim 1762, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagenic compound, a fluorescent compound and a chemiluminescent compound.

1841. (NEW) The system of claim 1801, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagen compound, a fluorescent compound and a chemiluminescent compound.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 47 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1842. (NEW) The system of claim 1762, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

1843. (NEW) The system of claim 1801, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

1844. (NEW) The system of claim 1762, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

1845. (NEW) The system of claim 1801, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

1846. (NEW) The system of claim 1844, wherein said colored compound comprises a dye.

1847. (NEW) The system of claim 1845, wherein said colored compound comprises a dye.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 48 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1848. (NEW) The system of claim 1762, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

1849. (NEW) The system of claim 1801, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

1850. (NEW) The system of claim 1848, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

1851. (NEW) The system of claim 1849, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

1852. (NEW) The system of claim 1762, wherein said non-porous solid support is transparent or translucent.

1853. (NEW) The system of claim 1762, wherein said activated surface is transparent or translucent.

1854. (NEW) The system of claim 1762, wherein said system is transparent or translucent.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 49 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1855. (NEW) The system of claim 1762, wherein said system retains or contains a fluid or solution.

1856. (NEW) The system of claim 1762, wherein said system and said solid support are composed of the same material.

1857. (NEW) The system of claim 1762, wherein said system functions as said solid support.

1858. (NEW) The system of claim 1762, comprising more than one double-stranded nucleic acid strands or sequences fixed or immobilized to said activated surface.

1859. (NEW) A non-porous system which comprises:

a non-porous solid support having an activated surface; and
at least one single-stranded nucleic acid strand or sequence fixed or immobilized to said solid support surface covalently or non-covalently through said activated surface.

1860. (NEW) The system of claim 1859, wherein said non-porous solid support comprises siliceous matter or polymeric material.

1861. (NEW) The system of claim 1860, wherein said siliceous matter comprises glass.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 50 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1862. (NEW) The system of claim 1861, wherein said glass is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

1863. (NEW) The system of claim 1862, wherein said plate or plates comprise microtiter well plates.

1864. (NEW) The system of claim 1862, wherein said wells comprise microtiter wells.

1865. (NEW) The system of claim 1861, wherein said glass comprises porous glass or porous glass beads.

1866. (NEW) The system of claim 1860, wherein said non-porous polymeric substrate comprises plastic.

1867. (NEW) The system of claim 1866, wherein said plastic is selected from the group consisting of polyethylene, polypropylene, polystyrene and polyepoxide.

1868. (NEW) The system of claim 1866, wherein said plastic is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection of said plates, wells, depressions, tubes, cuvettes or beads.

1869. (NEW) The system of claim 1868, wherein said plate or plates comprise polystyrene plates.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 51 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1870. (NEW) The system of claim 1868, wherein said wells comprise microtiter wells.

1871. (NEW) The system of claim 1868, wherein said wells comprise polystyrene microfilter wells.

1872. (NEW) The system of claim 1868, wherein said wells comprise removeable wells.

1873. (NEW) The system of claim 1859, wherein said activated surface has been treated with a surface treatment agent.

1874. (NEW) The system of claim 1873, wherein said surface treatment agent is selected from the group consisting of an amine compound and an epoxy resin or solution.

1875. (NEW) The system of claim 1874, wherein said amine compound comprises an amino-substituted hydrophobic polymer.

1876. (NEW) The system of claim 1874, wherein said amine compound is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

1877. (NEW) The system of claim 1874, wherein said amine compound comprises polylysine (PPL).

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 52 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1878. (NEW) The system of claim 1873, wherein said surface treatment agent comprises an epoxy resin or solution.

1879. (NEW) The system of claim 1859, wherein said activated surface comprises one or more amine, polyamine, amino-substituted or amino-derivitized groups thereon.

1880. (NEW) The system of claim 1879, wherein said amine, polyamine, amino-substituted or amino-derivitized group or groups result from a treatment of said activated surface with a surface treatment agent.

1881. (NEW) The system of claim 1880, wherein said surface treatment agent is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

1882. (NEW) The system of claim 1859, wherein said at least one nucleic acid strand or sequence has been fixed or immobilized to an amine or polyamine on said activated surface.

1883. (NEW) The system of claim 1859, wherein said activated surface has been treated with a blocking agent.

1884. (NEW) The system of claim 1883, wherein said blocking agent comprises Denhardt's solution.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 53 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1885. (NEW) The system of claim 1859, wherein said at least one nucleic acid strand or sequence has been fixed or immobilized directly or indirectly to said activated surface.

1886. (NEW) The system of claim 1885, wherein said direct or indirect fixation or immobilization to said activated surface is covalent or noncovalent.

1887. (NEW) The system of claim 1859, wherein said single-stranded nucleic acid strand or sequence is selected from the group consisting of DNA and RNA.

1888. (NEW) The system of claim 1859, wherein said at least one single-stranded nucleic acid strand or sequence comprises a nucleic acid sequence complementary to a nucleic acid sequence of interest or sought to be identified or quantified or sequenced.

1889. (NEW) The system of claim 1888, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises a member selected from the group consisting of a gene or gene sequence, a pathogen or pathogenic sequence, and a combination of any of the foregoing.

1890. (NEW) The system of claim 1888, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 54 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1891. (NEW) The system of claim 1888, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced is isolated or derived from a biological or non-biological sample.

1892. (NEW) The system of claim 1891, wherein said biological sample comprises blood, urine, feces, saliva, pus, semen, serum or tissue.

1893. (NEW) The system of claim 1891, wherein said non-biological sample comprises fermentation broth or culture media.

1894. (NEW) The system of claim 1888, wherein said complementary nucleic acid sequence or sequences are unlabeled.

1895. (NEW) The system of claim 1890, wherein said non-radioactive chemical label or labels are the non-radioactive signaling moiety or moieties.

1896. (NEW) The system of claim 1890, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 55 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1897. (NEW) The system of claim 1895, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1898. (NEW) The system of claim 1890, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

1899. (NEW) The system of claim 1895, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

1900. (NEW) The system of claim 1890, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

1901. (NEW) The system of claim 1895, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

1902. (NEW) The system of claim 1900, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 56 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1903. (NEW) The system of claim 1901, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

1904. (NEW) The system of claim 1902, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1905. (NEW) The system of claim 1903, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

1906. (NEW) The system of claim 1904, wherein said bridging entity or complex is covalently or non-covalently attached.

1907. (NEW) The system of claim 1905, wherein said bridging entity or complex is covalently or non-covalently attached.

1908. (NEW) The system of claim 1906, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

1909. (NEW) The system of claim 1907, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 57 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1910. (NEW) The system of claim 1890, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are covalently or non-covalently attached thereto.

1911. (NEW) The system of claim 1890, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are directly attached thereto.

1912. (NEW) The system of claim 1890, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are indirectly attached thereto.

1913. (NEW) The system of claim 1890, wherein said non-radioactive chemical label or labels comprise biotin, iminobiotin, a hapten or a ligand.

1914. (NEW) The system of claim 1890, wherein said non-radioactive chemical label or labels comprise indicator molecules.

1915. (NEW) The system of claim 1914, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1916. (NEW) The system of claim 1895, wherein said non-radioactive chemical label or labels comprise indicator molecules.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 58 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1917. (NEW) The system of claim 1916, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

1918. (NEW) The system of claim 1890, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive signaling moiety or moieties.

1919. (NEW) The system of claim 1895, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive chemical label or labels.

1920. (NEW) The system of claim 1890, wherein said non-radioactive signaling moiety or moieties are directly produced.

1921. (NEW) The system of claim 1920, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and chemiluminescent compound.

1922. (NEW) The system of claim 1890, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1923. (NEW) The system of claim 1922, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 59 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1924. (NEW) The system of claim 1923, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1925. (NEW) The system of claim 1924, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1926. (NEW) The system of claim 1925, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

1927. (NEW) The system of claim 1895, wherein said non-radioactive signaling moiety or moieties are directly produced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 60 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1928. (NEW) The system of claim 1927, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and chemiluminescent compound.

1929. (NEW) The system of claim 1895, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

1930. (NEW) The system of claim 1929, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

1931. (NEW) The system of claim 1930, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

1932. (NEW) The system of claim 1931, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

1933. (NEW) The system of claim 1932, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

1934. (NEW) The system of claim 1890, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagenic compound, a fluorescent compound and a chemiluminescent compound.

1935. (NEW) The system of claim 1895, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagen compound, a fluorescent compound and a chemiluminescent compound.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 62 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

936. (NEW) The system of claim 1890, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

937. (NEW) The system of claim 1895, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

938. (NEW) The system of claim 1890, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

939. (NEW) The system of claim 1895, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

940. (NEW) The system of claim 1938, wherein said colored compound comprises a dye.

941. (NEW) The system of claim 1939, wherein said colored compound comprises a dye.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 63 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1942. (NEW) The system of claim 1890, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

1943. (NEW) The system of claim 1895, wherein a non-radioactive signal from said non-radioactive chemical label or labels is quantifiable or detectable by photometric means.

1944. (NEW) The system of claim 1942, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

1945. (NEW) The system of claim 1943, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

1946. (NEW) The system of claim 1859, wherein said non-porous solid support is transparent or translucent.

1947. (NEW) The system of claim 1859, wherein said activated surface is transparent or translucent.

1948. (NEW) The system of claim 1859, wherein said system is transparent or translucent.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 64 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1949. (NEW) The system of claim 1859, wherein said system retains or contains a fluid or solution.

1950. (NEW) The system of claim 1859, wherein said system and said solid support are composed of the same material.

1951. (NEW) The system of claim 1859, wherein said system functions as said solid support.

1952. (NEW) The system of claim 1859, further comprising a second nucleic acid strand or sequence hybridized to said single-stranded nucleic acid strand or sequence fixed or immobilized to said activated surface.

1953. (NEW) A non-porous system which comprises:

a non-porous solid support comprising a surface which comprises one or more amine or polyamine or amino-derivatized or amino-substituted groups thereon; and

at least one double-stranded nucleic acid strand or sequence fixed or immobilized to said solid support surface covalently or non-covalently through said amine or polyamine or amino-derivitized or amino-substituted group or groups, wherein said at least one nucleic acid strand or sequence comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 65 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1954. (NEW) The system of claim 1953, wherein said non-porous solid support comprises siliceous matter or polymeric material.

1955. (NEW) The system of claim 1954, wherein said siliceous matter comprises glass.

1956. (NEW) The system of claim 1955, wherein said glass is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

1957. (NEW) The system of claim 1956, wherein said plate or plates comprise microtiter well plates.

1958. (NEW) The system of claim 1956, wherein said wells comprise microtiter wells.

1959. (NEW) The system of claim 1955, wherein said glass comprises porous glass or porous glass beads.

1960. (NEW) The system of claim 1954, wherein said polymeric material comprises plastic.

1961. (NEW) The system of claim 1960, wherein said plastic is selected from the group consisting of polyethylene, polypropylene, polystyrene and polyepoxide.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 66 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1962. (NEW) The system of claim 1960, wherein said plastic is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

1963. (NEW) The system of claim 1962, wherein said plate or plates comprises polystyrene plates.

1964. (NEW) The system of claim 1962, wherein said wells comprise microtiter wells.

1965. (NEW) The system of claim 1962, wherein said wells comprise polystyrene microfilter wells.

1966. (NEW) The system of claim 1962, wherein said wells comprise removeable wells.

1967. (NEW) The system of claim 1953, wherein said surface has been treated with a surface treatment agent.

1968. (NEW) The system of claim 1967, wherein said surface treatment agent is selected from the group consisting of an amine compound and an epoxy resin or solution.

1969. (NEW) The system of claim 1968, wherein said amine compound comprises an amino-substituted hydrophobic polymer.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 67 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1970. (NEW) The system of claim 1968, wherein said amine compound is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution, and a combination of any of the foregoing.

1971. (NEW) The system of claim 1968, wherein said amine compound comprises polylysine (PPL).

1972. (NEW) The system of claim 1967, wherein said surface treatment agent comprises an epoxy resin or solution.

1973. (NEW) The system of claim 1953, wherein said amine, polyamine, amino-substituted or amino-derivitized group or groups result from a treatment of said surface with a surface treatment agent.

1974. (NEW) The system of claim 1973, wherein said surface treatment agent is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

1975. (NEW) The system of claim 1953, wherein said at least one double-stranded nucleic acid strand or sequence has been fixed or immobilized to an amine or polyamine on said surface.

1976. (NEW) The system of claim 1953, wherein said surface has been treated with a blocking agent.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 68 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1977. (NEW) The system of claim 1976, wherein said blocking agent comprises Denhardt's solution.

1978. (NEW) The system of claim 1953, wherein said at least one nucleic acid strand or sequence has been fixed or immobilized directly or indirectly to said surface.

1979. (NEW) The system of claim 1953, wherein one strand of said at least one double-stranded nucleic acid strand or sequence is fixed or immobilized directly or indirectly to said surface.

1980. (NEW) The system of claim 1979, wherein said direct or indirect fixation or immobilization to said surface is covalent or noncovalent.

1981. (NEW) The system of claim 1953, wherein one strand of said at least one double-stranded nucleic acid or sequence is fixed or immobilized to said surface and the other strand is hybridized to said fixed or immobilized one strand.

1982. (NEW) The system of claim 1953, wherein said at least one double-stranded nucleic acid strand or sequence is fixed or immobilized to said surface by sandwich hybridization.

1983. (NEW) The system of claim 1953, wherein said at least one double-stranded nucleic acid strand or sequence is selected from the group consisting of DNA, RNA and a DNA-RNA hybrid.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 69 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1984. (NEW) The system of claim 1953, wherein said at least one nucleic acid strand or sequence comprises a nucleic acid sequence complementary to a nucleic acid sequence of interest or sought to be identified or quantified or sequenced.

1985. (NEW) The system of claim 1984, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced is isolated or derived from a biological or non-biological sample.

1986. (NEW) The system of claim 1985, wherein said biological sample comprises blood, urine, feces, saliva, pus, semen, serum or tissue.

1987. (NEW) The system of claim 1985, wherein said non-biological sample comprises fermentation broth or culture media.

1988. (NEW) The system of claim 1984, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises a member selected from the group consisting of a gene or gene sequence, a pathogen or pathogenic sequence, and a combination of any of the foregoing.

1989. (NEW) The system of claim 1984, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable.

1990. (NEW) The system of claim 1984, wherein said complementary nucleic acid sequence or sequences are unlabeled.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 70 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1991. (NEW) The system of claim 1953, wherein said non-radioactive chemical label or labels are the non-radioactive signaling moiety or moieties.

1992. (NEW) The system of claim 1953, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1993. (NEW) The system of claim 1991, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

1994. (NEW) The system of claim 1953, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

1995. (NEW) The system of claim 1991, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 71 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

1996. (NEW) The system of claim 1953, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

1997. (NEW) The system of claim 1991, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

1998. (NEW) The system of claim 1996, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

1999. (NEW) The system of claim 1997, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

2000. (NEW) The system of claim 1998, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

2001. (NEW) The system of claim 1999, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

2002. (NEW) The system of claim 2000, wherein said bridging entity or complex is covalently or non-covalently attached.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 72 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2003. (NEW) The system of claim 2001, wherein said bridging entity or complex is covalently or non-covalently attached.

2004. (NEW) The system of claim 2002, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

2005. (NEW) The system of claim 2003, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

2006. (NEW) The system of claim 1953, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are covalently or non-covalently attached thereto.

2007. (NEW) The system of claim 2006, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are directly attached thereto.

2008. (NEW) The system of claim 1953, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are indirectly attached thereto.

2009. (NEW) The system of claim 1953, wherein said non-radioactive chemical label or labels comprise biotin, iminobiotin, a hapten or a ligand.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 73 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2010. (NEW) The system of claim 1953, wherein said non-radioactive chemical label or labels comprise indicator molecules.

2011. (NEW) The system of claim 2010, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

2012. (NEW) The system of claim 1991, wherein said non-radioactive chemical label or labels comprise indicator molecules.

2013. (NEW) The system of claim 2012, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

2014. (NEW) The system of claim 1953, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive signaling moiety or moieties.

2015. (NEW) The system of claim 1991, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive chemical label or labels.

2016. (NEW) The system of claim 1953, wherein said non-radioactive signaling moiety or moieties are directly produced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 74 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2017. (NEW) The system of claim 2016, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and a chemiluminescent compound.

2018. (NEW) The system of claim 1953, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

2019. (NEW) The system of claim 2018, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

2020. (NEW) The system of claim 2019, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

2021. (NEW) The system of claim 2020, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

2022. (NEW) The system of claim 2021, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

2023. (NEW) The system of claim 1991, wherein said non-radioactive signaling moiety or moieties are directly produced.

2024. (NEW) The system of claim 2023, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and a chemiluminescent compound.

2025. (NEW) The system of claim 1991, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 76 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2026. (NEW) The system of claim 2025, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

2027. (NEW) The system of claim 2026, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

2028. (NEW) The system of claim 2027, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

2029. (NEW) The system of claim 2028, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 77 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2030. (NEW) The system of claim 1953, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagenic compound, a fluorescent compound and a chemiluminescent compound.

2031. (NEW) The system of claim 1991, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagen compound, a fluorescent compound and a chemiluminescent compound.

2032. (NEW) The system of claim 1953, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

2033. (NEW) The system of claim 1991, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

2034. (NEW) The system of claim 1953, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 78 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2035. (NEW) The system of claim 1991, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

2036. (NEW) The system of claim 2034, wherein said colored compound comprises a dye.

2037. (NEW) The system of claim 2035, wherein said colored compound comprises a dye.

2038. (NEW) The system of claim 1953, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

2039. (NEW) The system of claim 1991, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

2040. (NEW) The system of claim 2038, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 79 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2041. (NEW) The system of claim 2039, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

2042. (NEW) The system of claim 1953, wherein said non-porous solid support is transparent or translucent.

2043. (NEW) The system of claim 1953, wherein said surface is transparent or translucent.

2044. (NEW) The system of claim 1953, wherein said system is transparent or translucent.

2045. (NEW) The system of claim 1953, wherein said system retains or contains a fluid or solution.

2046. (NEW) The system of claim 1953, wherein said system and said solid support are composed of the same material.

2047. (NEW) The system of claim 1953, wherein said system functions as said solid support.

2048. (NEW) The system of claim 1953, comprising more than one double-stranded nucleic acid strands or sequences fixed or immobilized to said surface.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 80 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2049. (NEW) A non-porous system which comprises:

a non-porous solid support comprising a surface which comprises one or more amine or polyamine or amino-derivitized or amino-substituted groups thereon; and

at least one single-stranded nucleic acid strand or sequence fixed or immobilized to said solid support surface covalently or non-covalently through said amine or polyamine or amino-derivitized or amino-substituted group or groups.

2050. (NEW) The system of claim 2049, wherein said non-porous solid support comprises siliceous matter or polymeric material.

2051. (NEW) The system of claim 2050, wherein said siliceous matter comprises glass.

2052. (NEW) The system of claim 2051, wherein said glass is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads and a collection or set of said plates, wells, depressions, tubes, cuvettes or beads.

2053. (NEW) The system of claim 2052, wherein said plate or plates comprise microtiter well plates.

2054. (NEW) The system of claim 2052, wherein said wells comprise microtiter wells.

2055. (NEW) The system of claim 2051, wherein said glass comprises porous glass or porous glass beads.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 81 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2056. (NEW) The system of claim 2050, wherein said non-porous polymeric substrate comprises plastic.

2057. (NEW) The system of claim 2056, wherein said plastic is selected from the group consisting of polyethylene, polypropylene, polystyrene and polyepoxide.

2058. (NEW) The system of claim 2056, wherein said plastic is selected from the group consisting of a plate, wells, depressions, tubes, cuvettes, beads, and a collection of said plates, wells, depressions, tubes, cuvettes or beads.

2059. (NEW) The system of claim 2058, wherein said plate or plates comprise polystyrene plates.

2060. (NEW) The system of claim 2058, wherein said wells comprise microtiter wells.

2061. (NEW) The system of claim 2058, wherein said wells comprise polystyrene microfilter wells.

2062. (NEW) The system of claim 2058, wherein said wells comprise removeable wells.

2063. (NEW) The system of claim 2049, wherein said surface has been treated with a surface treatment agent.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 82 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2064. (NEW) The system of claim 2063, wherein said surface treatment agent is selected from the group consisting of an amine compound and an epoxy resin or solution.

2065. (NEW) The system of claim 2064, wherein said amine compound comprises an amino-substituted hydrophobic polymer.

2066. (NEW) The system of claim 2064, wherein said amine compound is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

2067. (NEW) The system of claim 2064, wherein said amine compound comprises polylysine (PPL).

2068. (NEW) The system of claim 2063, wherein said surface treatment agent comprises an epoxy resin or solution.

2069. (NEW) The system of claim 2049, wherein said amine, polyamine, amino-substituted or amino-derivitized group or groups result from a treatment of said surface with a surface treatment agent.

2070. (NEW) The system of claim 2069, wherein said surface treatment agent is selected from the group consisting of duodecadiamine (DDA), polylysine (PPL), γ -aminopropyltriethoxysilane, ammonium acetate, epoxy resin or solution and a combination of any of the foregoing.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 83 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2071. (NEW) The system of claim 2049, wherein said at least one nucleic acid strand or sequence has been fixed or immobilized to an amine or polyamine on said surface.

2072. (NEW) The system of claim 2049, wherein said surface has been treated with a blocking agent.

2073. (NEW) The system of claim 2072, wherein said blocking agent comprises Denhardt's solution.

2074. (NEW) The system of claim 2049, wherein said at least one nucleic acid strand or sequence has been fixed or immobilized directly or indirectly to said surface.

2075. (NEW) The system of claim 2074, wherein said direct or indirect fixation or immobilization to said surface is covalent or noncovalent.

2076. (NEW) The system of claim 2049, wherein said single-stranded nucleic acid strand or sequence is selected from the group consisting of DNA and RNA.

2077. (NEW) The system of claim 2049, wherein said at least one single-stranded nucleic acid strand or sequence comprises a nucleic acid sequence complementary to a nucleic acid sequence of interest or sought to be identified or quantified or sequenced.

2078. (NEW) The system of claim 2077, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises a member selected from the group consisting of a gene or gene sequence, a pathogen or pathogenic sequence, and a combination of any of the foregoing.

2079. (NEW) The system of claim 2077, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced comprises one or more non-radioactive chemical labels which comprise a non-radioactive signaling moiety or moieties which are quantifiable or detectable.

2080. (NEW) The system of claim 2077, wherein said nucleic acid sequence of interest or sought to be identified or quantified or sequenced is isolated or derived from a biological or non-biological sample.

2081. (NEW) The system of claim 2080, wherein said biological sample comprises blood, urine, feces, saliva, pus, semen, serum or tissue.

2082. (NEW) The system of claim 2080, wherein said non-biological sample comprises fermentation broth or culture media.

2083. (NEW) The system of claim 2077, wherein said complementary nucleic acid sequence or sequences are unlabeled.

2084. (NEW) The system of claim 2079, wherein said non-radioactive chemical label or labels are the non-radioactive signaling moiety or moieties.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 85 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2085. (NEW) The system of claim 2079, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

2086. (NEW) The system of claim 2084, wherein said non-radioactive chemical label or labels comprise a non-radioactive signaling moiety or moieties which are quantifiable in or from a fluid or solution or in or through said substrate or said surfaces or a system or a collection or set containing said system or said substrate or said surfaces, said quantity being proportional to the amount or quantity of said label or labels.

2087. (NEW) The system of claim 2079, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

2088. (NEW) The system of claim 2084, wherein said non-radioactive chemical label or labels are attached covalently to said at least one nucleic acid strand or sequence.

2089. (NEW) The system of claim 2079, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 86 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2090. (NEW) The system of claim 2084, wherein said non-radioactive chemical label or labels are attached directly or indirectly to said at least one nucleic acid strand or sequence.

2091. (NEW) The system of claim 2089, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

2092. (NEW) The system of claim 2090, wherein said direct or indirect attachment is through one or more nucleotides in said at least one nucleic acid strand or sequence.

2093. (NEW) The system of claim 2091, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

2094. (NEW) The system of claim 2092, wherein said attachment is indirectly through a bridging entity or a formation of a complex.

2095. (NEW) The system of claim 2093, wherein said bridging entity or complex is covalently or non-covalently attached.

2096. (NEW) The system of claim 2094, wherein said bridging entity or complex is covalently or non-covalently attached.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 87 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2097. (NEW) The system of claim 2095, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

2098. (NEW) The system of claim 2096, wherein said bridging entity or complex is selected from the group consisting of biotin and avidin, biotin and streptavidin, a sugar and a lectin, and an antigen and an antibody.

2099. (NEW) The system of claim 2079, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are covalently or non-covalently attached thereto.

2100. (NEW) The system of claim 2079, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are directly attached thereto.

2101. (NEW) The system of claim 2079, wherein said non-radioactive signaling moiety or moieties of said non-radioactive chemical label or labels are indirectly attached thereto.

2102. (NEW) The system of claim 2079, wherein said non-radioactive chemical label or labels comprise biotin, iminobiotin, a hapten or a ligand.

2103. (NEW) The system of claim 2079, wherein said non-radioactive chemical label or labels comprise indicator molecules.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 88 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2104. (NEW) The system of claim 2103, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

2105. (NEW) The system of claim 2084, wherein said non-radioactive chemical label or labels comprise indicator molecules:

2106. (NEW) The system of claim 2105, wherein said indicator molecules are selected from the group consisting of a chromagenic compound, a fluorescent compound, a chemiluminescent compound and a combination of any of the foregoing.

2107. (NEW) The system of claim 2079, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive signaling moiety or moieties.

2108. (NEW) The system of claim 2084, wherein a quantifiable or detectable non-radioactive signal is generated or generatable directly or indirectly from said non-radioactive chemical label or labels.

2109. (NEW) The system of claim 2079, wherein said non-radioactive signaling moiety or moieties are directly produced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 89 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2110. (NEW) The system of claim 2109, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and chemiluminescent compound.

2111. (NEW) The system of claim 2079, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

2112. (NEW) The system of claim 2111, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

2113. (NEW) The system of claim 2112, wherein said enzyme or enzymatic reaction is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

2114. (NEW) The system of claim 2113, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

2115. (NEW) The system of claim 2114, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzothiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

2116. (NEW) The system of claim 2084, wherein said non-radioactive signaling moiety or moieties are directly produced.

2117. (NEW) The system of claim 2116, wherein said directly produced non-radioactive signaling moiety or moieties comprise a member selected from the group consisting of a chromagen, a fluorogen and chemiluminescent compound.

2118. (NEW) The system of claim 2084, wherein said non-radioactive signaling moiety or moieties are indirectly produced.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 91 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2119. (NEW) The system of claim 2118, wherein said non-radioactive signaling moiety or moieties are indirectly produced by an enzyme or enzymatic reaction.

2120: (NEW) The system of claim 2119, wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase, peroxidase, β -D-galactosidase and glucose oxidase.

2121. (NEW) The system of claim 2120, wherein said enzyme or enzymatic reaction fluoresces or produces a color change upon contact with a chromogen.

2122. (NEW) The system of claim 2121, wherein said chromogen comprises 4-methylumbelliferyl phosphate when said enzyme comprises alkaline phosphatase, wherein said chromogen comprises bis(4-methylumbelliferyl) phosphate, 3-O-methylfluorescein, flavone-3-diphosphate triammonium salt, or *p*-nitrophenyl phosphate 2Na when said enzyme comprises acid phosphatase, wherein said chromogen comprises tyramine hydrochloride, 3-(*p*-hydroxyphenyl) propionic acid, *p*-hydroxyphenethyl alcohol, 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS), *o*-phenylenediamine 3HCl, *o*-dianisidine, 5-aminosalicylic acid, *p*-cresol, 3,3'-dimethyloxybenzidine, 3-methyl-2-benzthiazoline hydrazone or tetramethyl benzidine when said enzyme comprise peroxidase, wherein said chromogen comprises *o*-nitrophenyl β -D-galactopyranoside or 4-methylumbelliferyl- β -D-galactoside when said enzyme comprises β -D-galactosidase, and wherein said chromogen comprises 2'2'-azino-di-3-ethylbenzthiazoline sulfonic acid (ABTS) when said enzyme comprises glucose oxidase.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 92 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2123. (NEW) The system of claim 2079, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagenic compound, a fluorescent compound and a chemiluminescent compound.

2124. (NEW) The system of claim 2084, wherein said non-radioactive signaling moiety or moieties are selected from the group consisting of an enzyme, a co-enzyme, a chelating compound, a chromagen compound, a fluorescent compound and a chemiluminescent compound.

2125. (NEW) The system of claim 2079, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

2126. (NEW) The system of claim 2084, wherein a non-radioactive signal is generated or generatable from said non-radioactive chemical label or labels by a means selected from the group consisting of chromagenic means, fluorescent means and chemiluminescent means.

2127. (NEW) The system of claim 2079, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

2128. (NEW) The system of claim 2084, wherein said non-radioactive chemical label or labels are selected from the group consisting of a colored compound, a chemiluminescent compound and a fluorescent compound.

2129. (NEW) The system of claim 2127, wherein said colored compound comprises a dye.

2130. (NEW) The system of claim 2128, wherein said colored compound comprises a dye.

2131. (NEW) The system of claim 2079, wherein a non-radioactive signal from said non-radioactive signaling moiety or moieties is quantifiable or detectable by photometric means.

2132. (NEW) The system of claim 2084, wherein a non-radioactive signal from said non-radioactive chemical label or labels is quantifiable or detectable by photometric means.

2133. (NEW) The system of claim 2131, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 94 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2134. (NEW) The system of claim 2132, wherein said photometric means are selected from the group consisting of photometric techniques, spectrophotometric techniques, colorimetric techniques, fluorometric techniques and chemiluminescent techniques.

2135. (NEW) The system of claim 2049, wherein said non-porous solid support is transparent or translucent.

2136. (NEW) The system of claim 2049, wherein said surface is transparent or translucent.

2137. (NEW) The system of claim 2049, wherein said system is transparent or translucent.

2138. (NEW) The system of claim 2049, wherein said system retains or contains a fluid or solution.

2139. (NEW) The system of claim 2049, wherein said system and said solid support are composed of the same material.

2140. (NEW) The system of claim 2049, wherein said system functions as said solid support.

2141. (NEW) The system of claim 2049, comprising more than one single-stranded nucleic acid strand or sequence fixed or immobilized to said solid support surface.

Jannis G. Stavrianopoulos et al.

Serial No.: 08/486,070

Filed: June 7, 1995

Page 95 [Supplemental Amendment to Applicants' April 10, 2002 Amendment
Under 37 C.F.R. §1.116 -- June 17, 2002]

2142. (NEW) The system of claim 2049, further comprising a second nucleic acid strand or sequence hybridized to said at least one single-stranded nucleic acid strand or sequence fixed or immobilized to said solid support surface.

* * * * *